PATENT

Docket No. 43682USA5C

#5
9/2/92

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

STEVEN M. WICK, HELEN JENSEN SCHULTZ, GREGORY R. NELSON, AMIT K. MITRA AND STEPHEN M. BERGE

Serial No.: 07/845,323

Filed: March 3, 1992

For: TOPICAL FORMULATIONS AND TRANSDERMAL DELIVERY SYSTEMS CONTAINING 1-ISOBUTYL-1H-IMIDAZO-[4,5-C]QUINOLIN-4-AMINE

Examiner: R. Henley III

Group Art Unit: 1205

AFFIDAVIT OF STEPHEN M. BERGE UNDER 37 CFR §1.132

STATE OF MINNESOTA)
) ss.
COUNTY OF RAMSEY)

1. I am the Stephen M. Berge named as an inventor of the subject application.

2. I received a Bachelor of Science degree in Pharmacy from the University of Iowa in the year 1973, and I received a Doctor of Philosophy degree in Pharmaceutics from the University of Iowa in the year 1978.

3. I have been employed in the pharmaceutical industry since the year 1978 and by Minnesota Mining and Manufacturing Company since the year 1986, during which time I have been actively engaged in research in the field of pharmaceutical dosage form design and development including topical, transdermal, injectable, and oral solid and liquid dosage forms.

4. I directed a series of experiments in order to determine and evaluate the effect of certain fatty acids on the transdermal drug delivery characteristics of formulations containing 1-isobutyl-1H-imidazo[4,5-c]quinolin-4-amine.

Five fatty acids were used: oleic acid and isostearic acid for use in formulations of the invention, and linoleic acid, palmitic acid, and stearic acid for use in comparative examples.

The formulations were prepared according to Example 13 of the subject application, using one of the several fatty acids at concentrations of 5%, 25%, and 40% by weight. Example 13 uses 25% by weight of isostearic acid. In the 5% and 40% formulations, the amount of water was adjusted to account for the excess or deficiency of the fatty acid.

The 25% isostearic acid formulation differs from the others in that it contains 0.5% by weight xanthan gum.

Delivery data were obtained at 4, 7, and 24 hours in the In Vitro Test Method set forth at page 15, line 17 of the specification.

The results are set forth in TABLE 1 below. The numbers represent the average of 3 independent HPLC determinations of the amount of drug in the receptor solution (μg/mL). Standard deviation is set forth in parenthesis.

The data in TABLE I show that over a period of 24 hours the formulations containing isostearic acid and oleic acid deliver considerably more drug across hairless mouse skin in the In Vitro Test Method than the formulations containing palmitic acid or stearic acid. It is my opinion that the stearic acid and palmitic acid formulations are unsuitable for use in delivering 1-isobutyl-1H-imidazo[4,5-c]quinolin-4-amine across the skin. Furthermore, the palmitic acid and stearic acid formulations formed relatively hard white pastes that are not optimal for use as topical formulations.

The data in TABLE I also show that the formulations containing linoleic acid afford suitable drug delivery characteristics in the In Vitro Test method. Also, these formulations were not unsuitably viscous for use as topical formulations.

Further Affiant sayeth not.

Stephen M. Berge

Stephen M. Berge

Subscribed and sworn to before me this 21 day of August 1992.

Lou A. Marschke

Notary Public

LOU A. MARSCHKE
NOTARY PUBLIC—MINNESOTA
WASHINGTON COUNTY
My Comm. Expires April 24, 1995

DER/mlh
43682-5C.AFF

TABLE I

Comparative Examples
Active Ingredient Concentration in Receptor Solution (μg/mL)

	Oleic Acid			Isostearic Acid			Linoleic Acid			Palmitic Acid			Stearic Acid		
	5%	25%	40%	5%	25%	40%	5%	25%	40%	5%	25%	40%	5%	25%	40%
4h	0.30 (0.06)	2.36 (1.0)	4.76 (2.52)	0.28 (0.13)	2.36 (0.18)	3.65 (0.85)	0.72 (0.79)	2.94 (1.65)	4.52 (0.55)	0.59 (0.50)	0.13 (0.23)	0.17 (0.17)	0.24 (0.20)	0.22 (0.38)	0.056 (0.10)
7h	0.49 (0.13)	3.33 (1.54)	7.33 (2.48)	0.44 (0.26)	7.00 (0.38)	6.63 (2.51)	0.63 (0.50)	5.6 (0.71)	6.62 (0.84)	0.09 (0.08)	0.09 (0.02)	0 (0)	0.03 (0.05)	0 (0)	0 (0)
24h	9.8 (3.7)	88.5 (29.3)	108 (25.8)	6.1 (2.6)	121 (6.43)	116 (30.2)	7.5 (1.8)	96.1 (14.8)	107 (15.3)	0.78 (0.27)	0.74 (0.46)	0.67 (0.19)	0.50 (0.14)	1.05 (0.53)	1.23 (0.15)